

CLAIMS

1. A sensor device for determining the extent of aggregation of a protein in a fluid having a sensor component capable of exhibiting a measurable response to a change in a localised environment caused by the introduction of the fluid, wherein a surface of said sensor component exposed to the fluid is provided with a specific binding partner to the protein rendering the measurable response to the change in the localised environment discriminatory to the extent of aggregation of the protein.
2. A sensor device as claimed in claim 1 wherein the protein is beta amyloid.
3. A sensor device as claimed in claim 2 wherein the specific binding partner to beta amyloid is an optionally biotinylated antigen.
4. A sensor device as claimed in any preceding claim wherein the fluid is a bodily fluid.
5. A sensor device as claimed in any preceding claim wherein the sensor component is capable of exhibiting a measurable response in a parameter selected from effective refractive index, a dielectric constant, a viscoelastic property, a frequency of oscillation, a thermal absorption/desorption parameter, the permeability, the absorption of energy or of energetic particles or the particle size.
6. A sensor device as claimed in claim 5 wherein the parameter is the effective refractive index.
7. A sensor device as claimed in any preceding claim wherein the sensor component is derivatised for the purposes of attaching or absorbing the specific binding partner.
8. A sensor device as claimed in claim 7 wherein the surface of the sensor component comprises an absorbent material.
9. A sensor device as claimed in claim 7 wherein the surface of the sensor component comprises a porous silicon material capable of being biofunctionalised with the specific binding partner.
10. A sensor device as claimed in any preceding claim wherein the sensor component is a waveguide structure including:
either (a) one or more sensing layers capable of inducing in a secondary waveguide measurable response to a change in the localised environment caused by the introduction of the fluid;
or (b) a sensing waveguide capable of exhibiting a measurable response to a change in the localised environment caused by the introduction of the fluid.
11. A sensor device as claimed in any preceding claim wherein the sensor component is a waveguide structure including:
either (a) one or more sensing layers capable of inducing in a secondary waveguide a measurable response to a change in the localised environment caused by the introduction of the fluid and an inactive secondary waveguide in which the sensing layer is incapable of inducing a measurable response to a change in the localised environment caused by the introduction of the fluid or (b) a sensing waveguide capable of exhibiting a measurable response to a change in the localised

environment caused by the introduction of the fluid and an inactive waveguide substantially incapable of exhibiting a measurable response to a change in the localised environment caused by the introduction of the fluid.

12. A sensor device as claimed in claim 10 or 11 wherein the sensing waveguide or secondary waveguide of the sensor component is a planar waveguide.

13. A sensor device as claimed in claim 12 wherein each planar waveguide is a slab waveguide.

14. A method for determining the extent of aggregation of a protein in a fluid, said method comprising:

- (A) providing a sensor device as defined in any preceding claim;
- (B) irradiating the sensor component with electromagnetic radiation to generate an output;
- (C) introducing the fluid into the localised environment;
- (D) measuring the response of a characteristic of the output; and
- (E) relating the response of the characteristic of the output to the extent of aggregation of the protein.

15. A method as claimed in claim 14 wherein step (C) further comprises:

(C') introducing an amount of the specific binding partner into the localised environment.

16. A method as claimed in claim 14 or 15 wherein step (B) comprises:

(B') irradiating the sensor component with electromagnetic radiation to generate a first output;

(B'') measuring a characteristic of the first output;

and wherein steps (D) and (E) are:

(D) measuring the characteristic of the output relative to the characteristic of the first output; and

(E) relating the characteristic of the output relative to the characteristic of the first output to the extent of aggregation of the protein.

17. A method as claimed in any of claims 14 to 16 wherein the characteristic of the output is a positional characteristic.

18. A method as claimed in any of claims 14 to 17 wherein the output is a pattern of interference fringes.

19. A method as claimed in claim 18 wherein step (D) comprises: measuring movements in the pattern of interference fringes.

20. A method as claimed in claim 19 wherein step (D) further comprises: calculating the phase shift from the movements in the pattern of interference fringes.

21. A method as claimed in any of claims 18 to 20 wherein step (B) comprises:

(B1) irradiating the sensor component with electromagnetic radiation in TE mode to produce a first pattern of interference fringes;

(B2) irradiating the sensor component with electromagnetic radiation in TM mode to produce a second pattern of interference fringes;

and step (D) comprises:

- (D1) measuring movements in the first pattern of interference fringes; and
- (D2) measuring movements in the second pattern of interference fringes.

22. A method as claimed in claim 21 wherein step (D) further comprises:

- (D3) calculating the phase shift of the sensor component in TM mode from the movements in the first pattern of interference fringes;
- (D4) calculating the phase shift of the sensor component in TE mode from the movements in the second pattern of interference fringes;

and step (E) is

relating the phase shift of the sensor component in TM mode and the phase shift of the sensor component in TE mode to the extent of aggregation of the protein.

23. A method as claimed in claim 22 wherein step (D) further comprises:

- (D3) calculating the phase shift of the sensor component in TM mode from the movements in the first pattern of interference fringes

- (D4) calculating the phase shift of the sensor component in TE mode from the movements in the second pattern of interference fringes;

- (D5) calculating the phase shift of the sensor component in TM mode relative to the phase shift of the sensor component in TE mode;

and step (E) is

relating the phase shift of the sensor component in TM mode relative to the phase shift of the sensor component in TE mode to the extent of aggregation of the protein.

24. A method as claimed in claim 23 wherein the phase shift of the sensor component in TM mode relative to the phase shift of the sensor component in TE mode is a ratio of the phase shift of the sensor component in TM mode to the phase shift of the sensor component in TE mode.

25. A method as claimed in any of claims 14 to 24 further comprising:

- (F1) relating the response of the characteristic of the output to a change in the intrinsic refractive index and/or the volume;

- (F2) calculating the change in the molecular density; and

- (F3) optionally calculating the change in mass.

26. A kit of parts comprising:

a sensor device for determining the extent of aggregation of a protein in a fluid having a sensor component capable of exhibiting a measurable response to a change in a localised environment caused by the introduction of the fluid; and

a specific binding partner capable of binding to a surface of said sensor component so as to render the measurable response to a change in a localised environment discriminatory to the extent of aggregation of the protein.